# Neural interactions between anterior insula and anterior cingulate cortices link perceptual and physiological processes

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## Introduction

The bi-directional link between external sensory cues and bodily physiological adaptions represents a key function of the central nervous system. The salience brain network, anatomically anchored in the dorsal anterior cingulate cortex (ACC) and anterior insular cortex (AIC).

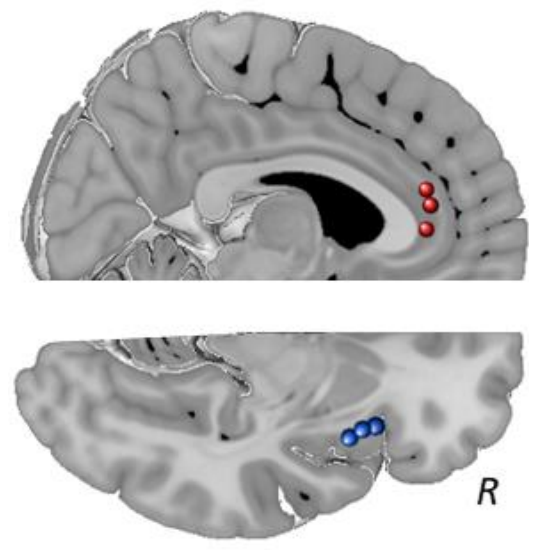
We investigated dynamic coupling between AIC and ACC using intracranial-EEG (stereo-EEG) depth recordings. We first show functional connectivity between the activity of these nodes using high frequency activity.

We then sought to understand feedforward and feedback interactions in AIC-ACC cortical circuit, i.e. effective connectivity using Dynamic Causal Modelling (DCM) for cross spectral density (CSD) with an underlying neuronal model of canonical microcircuit (CMC).

## Methods and Materials

Data from three patients with electrode implants in AIC and ACC who watched a 20 min short movie "The Butterfly Circus" participated in this study.

Anatomical locations of the electrode channels implanted in the ACC (the ventral portion of the cingulate gyrus, shown in red dots) and the AIC (anterior short gyrus, shown in blue dots) are shown in MNI space.




| P id | ROI | MNI x | MNI y | MNI z |
|---|---|---|---|---|
| P1 | ACC | 8 | 36 | 16 |
| P2 | ACC | 7 | 37 | 3 |
| P3 | ACC | 8 | 38 | 13 |
| P1 | AIC | 37 | 9 | -7 |
| P2 | AIC | 35 | 14 | -8 |
| P3 | AIC | 33 | 17 | 1 |

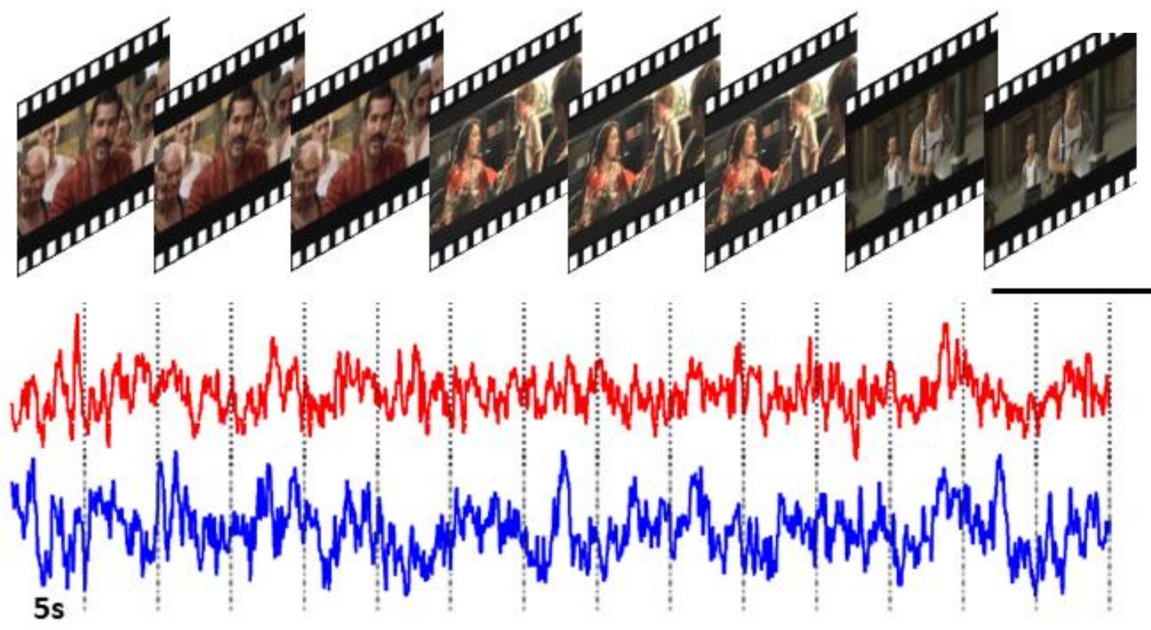
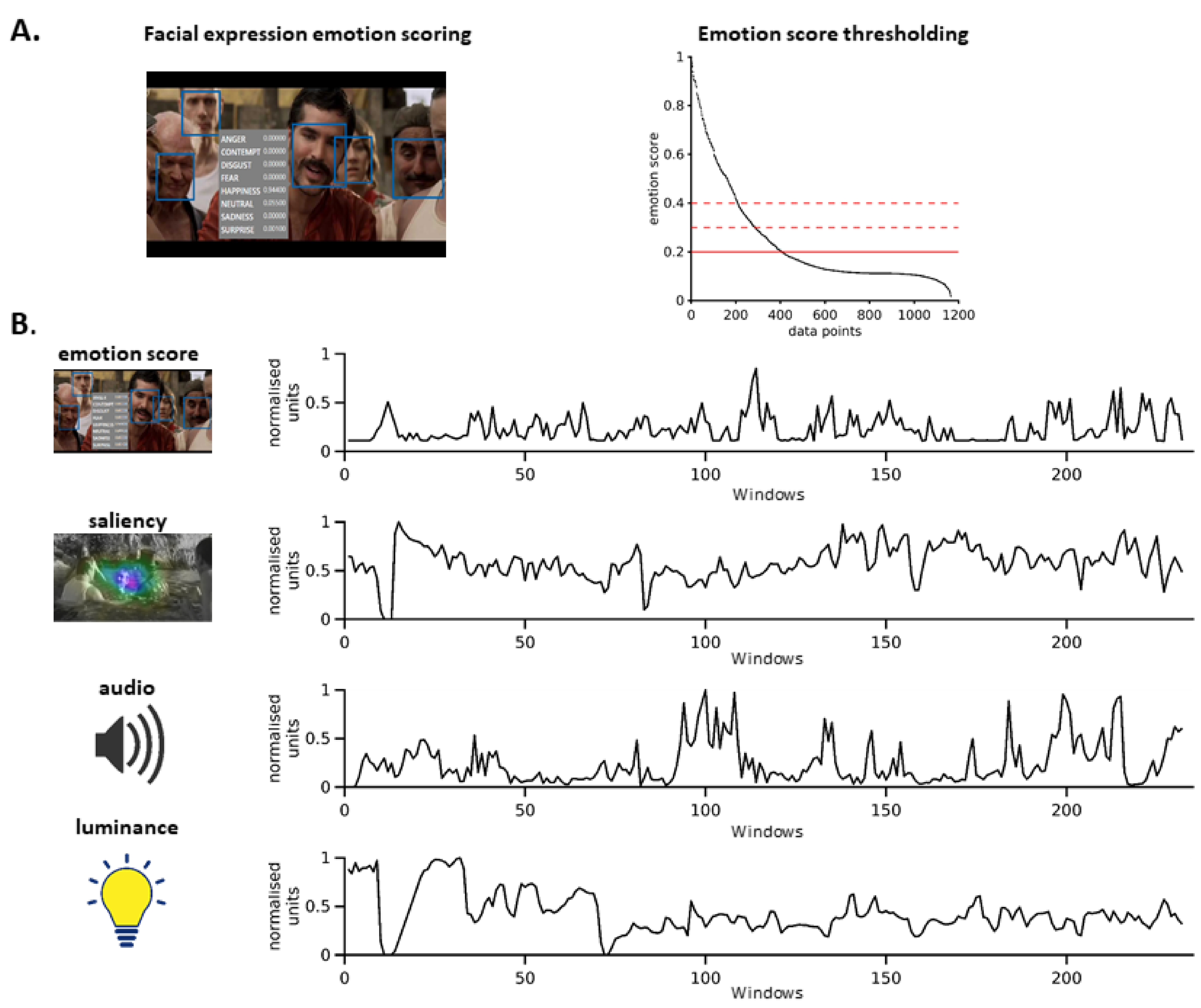



Illustration of movie scenes and time series of stereo-EEG recordings from the ACC and the AIC. Movie scenes and time series were segmented into 5-second windows based on the analysis of changes in global emotional scores across the movie frames (see text). The resulting 5-second time series data were each used to estimate dynamic changes in the AIC-ACC coupling separately.

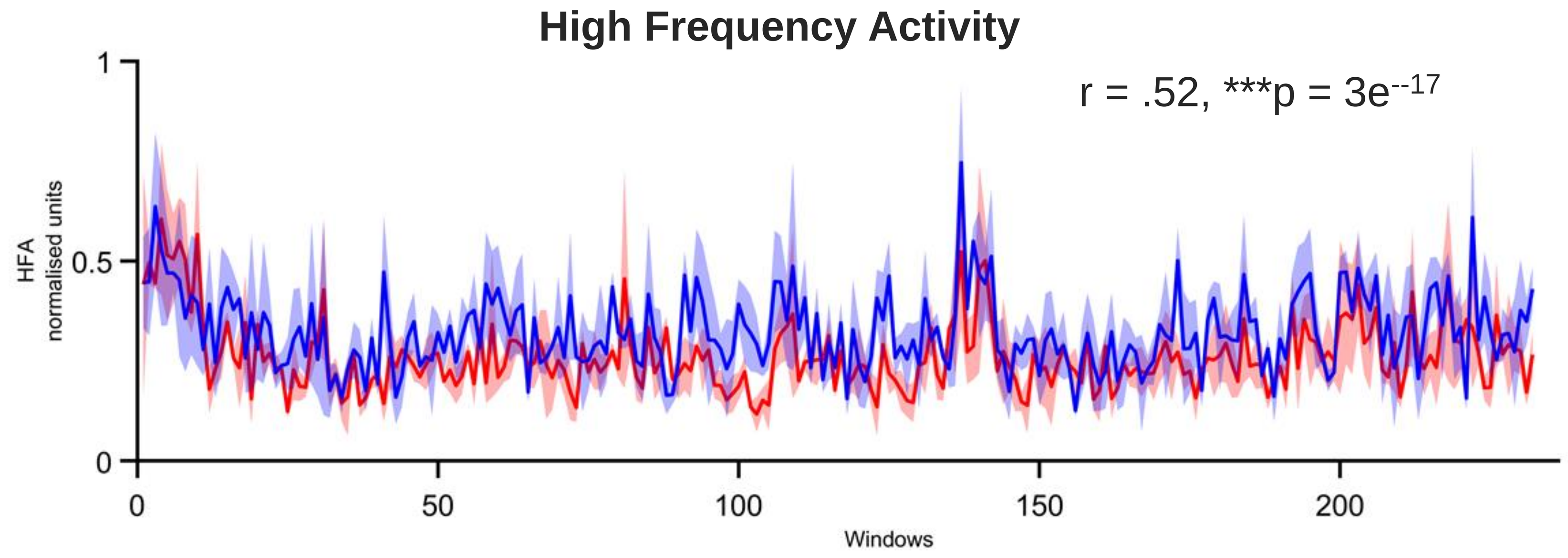
### Movie properties




**A:** *Left* - Facial expressions used to infer frame-wise emotional score; *Right* - the emotion scores of all the frames averaged for each second ranked in descending order. Note the discontinuities in the distribution as some emotion scores were not assigned to any frames. The solid red line shows the threshold of 0.2 used to compute the average emotional duration to segment data. The average emotional duration changed minimally when threshold values of 0.3 and 0.4 were used. **B:** Time series associated with movies features averaged for each of the 5-second windows to correspond to stereo-EEG data.

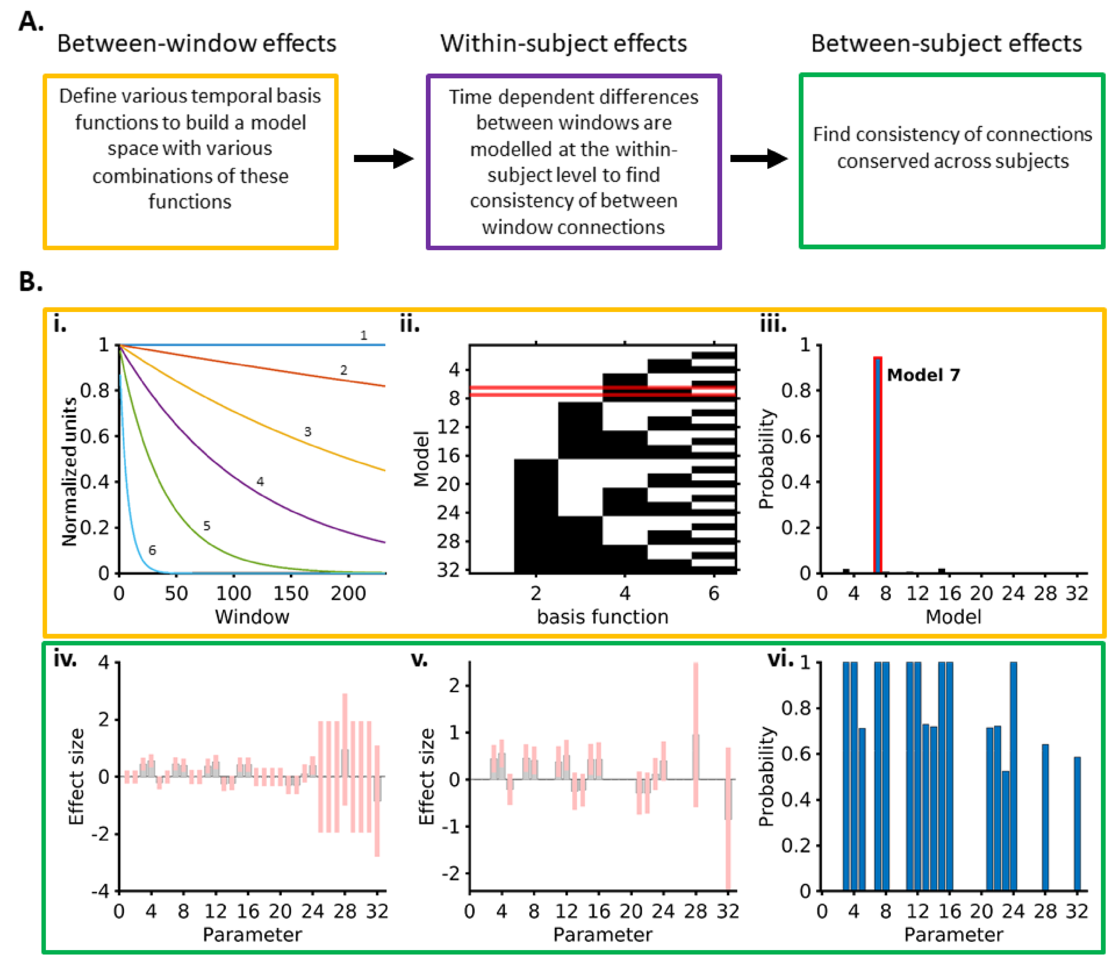
## Results

### High Frequency Activity



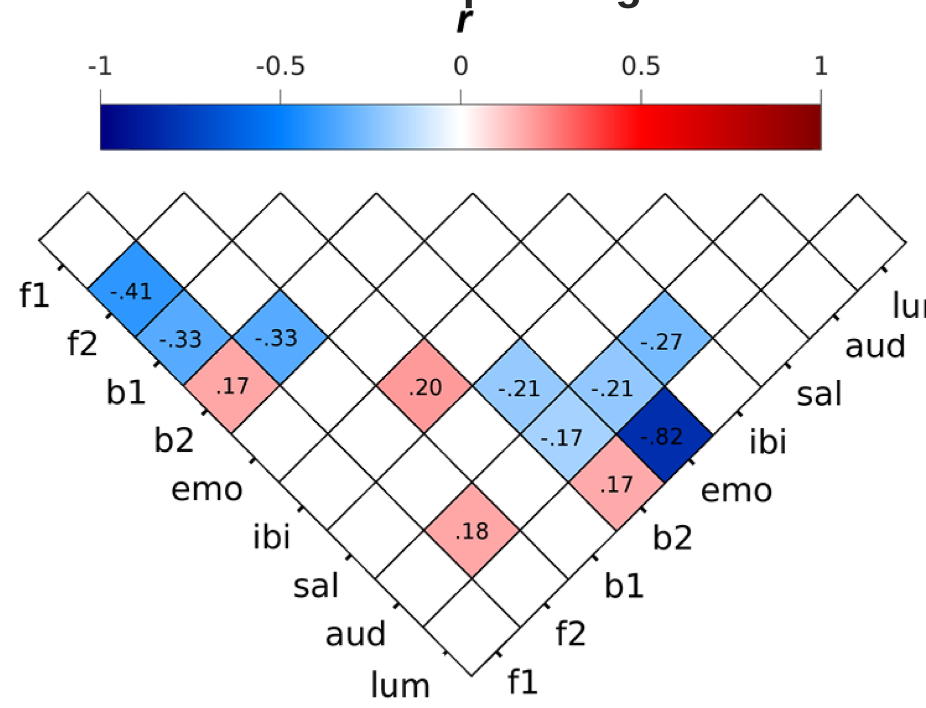

Time series showing group mean HFA of the ACC (blue) and AIC (red). Shading represents SEM. Highly correlated HFA fluctuations of the ACC and the AIC.

### Effective Connectivity Analyses




*Multi-level Parametric Empirical Bayes (PEB) analysis of effective connectivity parameters.* **A:** Overview of the different PEB analyses. **B i:** Regressors [a constant term (1) and five temporal basis functions (2,3,4,5,6)] considered in a Bayesian general linear model to estimate between-window consistency of effective connectivity parameters. **ii:** Model space with all possible combinations of the five temporal basis functions (with the constant term always included). White tiles indicate the presence of temporal basis basis functions in the model and the black tiles indicates their absence in the model. The winning model (seven) is highlighted in red. **iii:** Probability of winning model with Bayesian model comparison of all models. The winning model is highlighted in red and comprised of a combination of the constant term and three temporal basis functions (2,3 and 6 in panel A). **iv & v:** Group-PEB analysis. The plots show the connectivity parameters corresponding to models with the constant term (parameters 1-8) and each of the three winning temporal basis functions (parameters 9-32) and the related effect sizes. Pink bars denote 90% Bayesian confidence intervals. **vi:** Parameters reaching a posterior probability of 1were used for further analyses.

### Connectivity parameters and their association with exteroceptive and interoceptive signals




Pearson's correlation coefficient values (r) between connectivity parameters, IBI and movie features. f1 = feedforward connections from the ACC to the AIC, f2 = feedforward connections from the AIC to the ACC, b1 = feedback connections from AIC to ACC, b2 = feedback connections from the ACC to the AIC, emo – emotion scores, ibi – interbeat interval, sal – salience, aud – audio, lum – luminance. Correlations that survive multiple comparison correction (FDR) with a type I error probability of less than 5% are shown.

## Discussion

**1)** Time-resolved high-frequency neural activity in the AIC and ACC during movie viewing is strongly correlated, suggesting tight coupling between these two regions. Consequent **2)** Biophysical modelling extend these findings by showing that dynamic effective connectivity between the AIC and the ACC were (anti)correlated. Moreover, connectivity parameters from the ACC reflected extrinsic stimulus related sensory information, whereas that from the AIC were associated with both the stimulus properties as well as physiological responses. These results highlight the distinct - yet complementary - function of dynamical patterns of interactions between the AIC and the ACC.

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